

Disclosures

Leo Semes, OD, FAAO, FACMO
Speaker Bureau, Consultant - Maculogix
Speaker Bureau - Regeneron
Scientific Advisory Board - EyePromise
Stock options - Eye Promise (< 0.01% ownership),
HPO (< 0.01% ownership)

Following this course, the attendee should appreciate the unusual presentations of neovascular complications of retinal disorders other than AMD but including some apparently trivial presentations recognize the implications and management of ocular toxoplasmosis gain a new perspective on the potential sight-saving measures for infectious processes recognize that not all macular disorders involving neovascularization are amenable to treatment with an anti-VEGF agent

realize the potential prophylactic role of the OD in infectious maculopathies
 be able to triage macular disease for successful outcomes and appropriately counsel the patient with such presentations.

Disclaimer

"Half of what you'll learn during training will be shown to be either dead wrong or out-of-date within 5 years;

...the trouble is that nobody can tell you which half."

-David Sackett, MD

Widely regarded as the father of evidence-based medicine (1938-20)

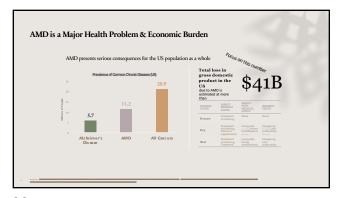
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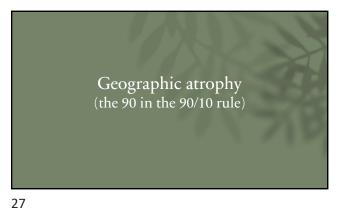
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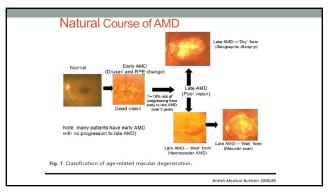
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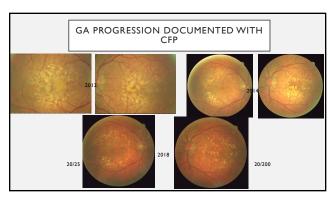


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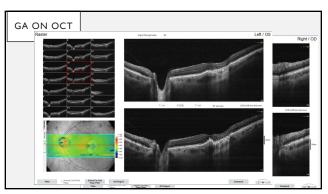








28 34



Let's look at pathogenesis of AMD, beginning with RPE

Role of retinal pigment epithelium in age-related macular disease: a systematic review

Alan Bird

James Age related macular disease: a systematic review

Alan Bird

James Age related macular disease: a systematic review

Alan Bird

James Age related macular disease (AMD) is a major cause of blinders and from a fill benefit to the control of early disease. Intraocular injection of artification for a distribution of early disease. Intraocular injection of artification of carry disease. Intraocular injection of artification of potential interpretative target of the correct, it would be concluded that despite major intraocular injection of artification of potential therapeutic variate before the carried or activity of artification of potential therapeutic variate before the activity of artification of potential therapeutic variate before the carried or marks the sauly of carry AMD and the distriction of potential therapeutic variate before the activity of the advanced interval to activity of the advanced interval to activity of the advanced interval to activity. In the page of the activity of the advanced interval to activity of the advanced interval to activity. In the page of the activi

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Conclusions

- The RPE is a critical nutritional transport element in the retina
- RPE stress may be the site of initial insult in all phenotypic expressions of AMD and may, therefore, serve as a potential therapeutic target
- The objective of such treatment would be restoration of lipid processing or energy restoration (think mitochondrial support)
- Mitochondrial-targeting peptides (e.g., elamipretide) are currently under investigation as is exposure to 670mn light
 Br J Ophthalmol; 2021 Nov 1; 105 (11)1469-1474

37 38

Pegcetacoplan (Apellis pharmaceuticals)

- Synthetic molecule that downregulates C3 and all complement pathways
- Delivered intravitreally
- Phase II Studies: 246 pts
- At 12 mos, 29% lower rate of GA progression with monthly injections vs sham
- · No difference in visual acuity

Targeting the complement pathway in GA LETIN Payantians in historical an international particular department of the complement cascade has been implicated in GA pathograess and the central cleavage of CA amplification top and the c

POTENTIALLY PROMISING

TREATMENTS

39

Pegcetacoplan

- Phase 3 DERBY and OAKS
- Sept 9, 2021
- · OAKS: met primary endpoint
- 16%-22% reduction in lesion growth at 1 year
- DERBY: did NOT meet primary endpoint
- 11%-12% reduction in lesion growth at 1 year
- Company moving forward
 Hopeful to submit 1st half 2022
- Hopeful approval end of 2022

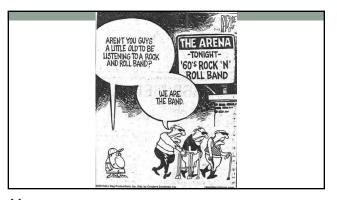
Would be first FDA approved treatment for dry AMD!!

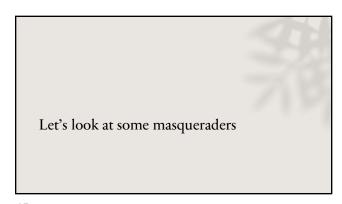
Gyroscope therapeutics

40

- GT005: investigational gene therapy designed to induce expression of CF-I after subretinal delivery
- · CF-I down regulates CF
- CF related to inflammation and GA lesion progression
- Stage II studies showed well tolerated and had positive effects on lesion size and acuity
- · Phase III studies underway
- Looking for pts with GA and CF-I rare variants (\cong 3-5%) vs all GA pts

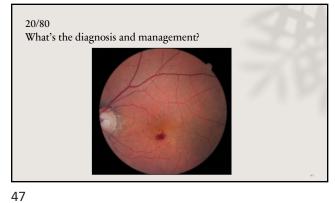
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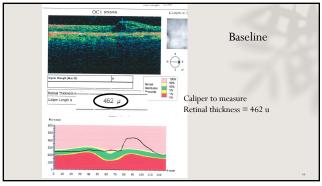


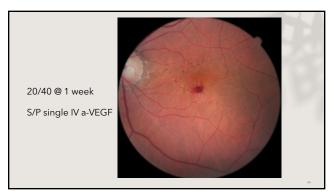
86 YOWM

- Presents with reduced VA OS
- POH: repaired peripheral retinal hole SN OS X 11 yrs
- Pseudophakic in each eye
- Medicated for HTn X 20 yrs

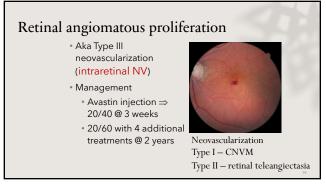


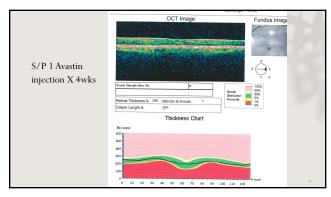
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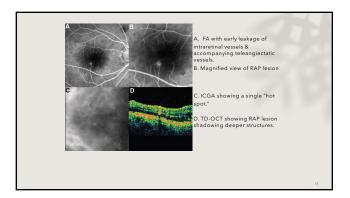


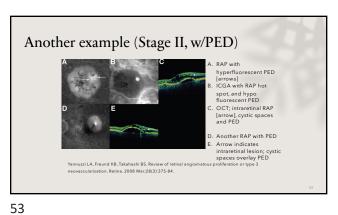


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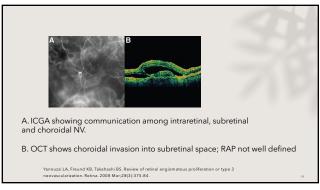


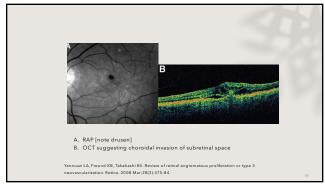




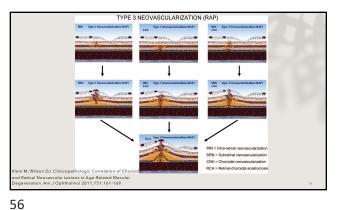


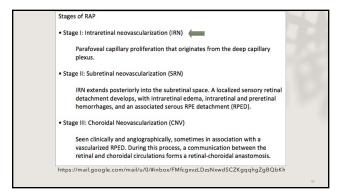
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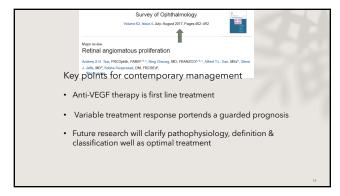




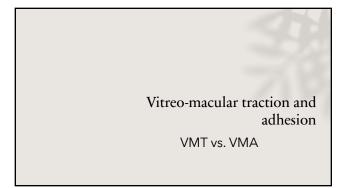
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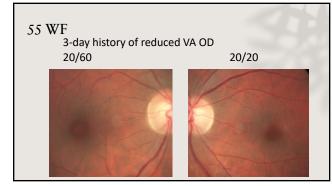


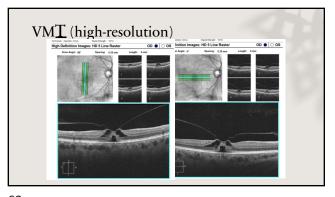


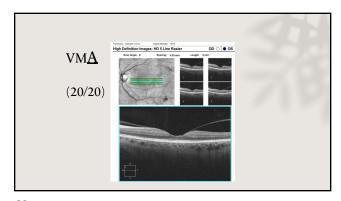


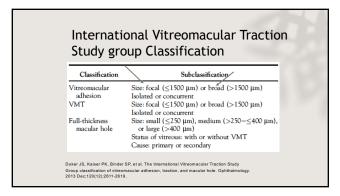


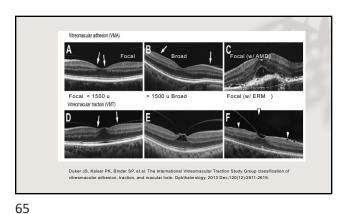












64 6.

Table 2. Correlation between Commonly Used Clinical Macular Hole Stages and the International Vitreomacular Traction Study Classification System for Vitreomacular Adhesion, Traction, and Macular Hole

Full-Thickness Macular Hole Stages in Common Use

International Vitreomacular Traction Study Classification System

Stage 0

Stage 1 impending macular hole

Stage 2 small hole

Stage 3 small hole

Stage 4 small hole

Stage 4 small hole

Stage 4 small hole

Medium or large FTMH with VMT

Stage 4 stage hole

Stage 1 mending macular hole, PVD = posterior vitrous detechment; VMA = vitreomacular adhesion; VMT = vitreomacular traction.

Duker JS, Kalser PK, Binder SP, et al. The International Vitreomacular Traction Study Group classification of vitreomacular adhesion, traction, and macular hole. Ophthalmology. 2013 Dec;120(12) 2611-2619.

Natural course of VMT

* 11% of 53 patients developed spontaneous PVD (& release of traction) at 60 months F/U

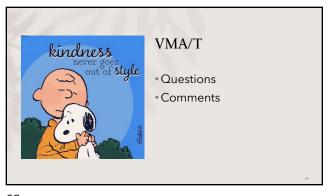
Hikichi T, Yoshida A, Akiba J, Tremps CL. Natural outcomes of stage 1, 2, 3, and 4 idiopathic macular holes. Br J Ophthalmal. 1995;79(6):
517-520.

* 32% of 106 symptomatic patients had spontaneous PVD at 23 months F/U

John VJ, Flynn HW Jr, Smiddy WE, et al. Clinical course of vitreomacular adhesion managed by initial observation. Retina. 2014

March;34(3):442-446.

66 67



Case shared by Dr. Steve Ferrucci

68 69

65 yo white male

• h/o OHS for many years

• Laser OD 20 + years ago with scarring and poor acuity ≈CF

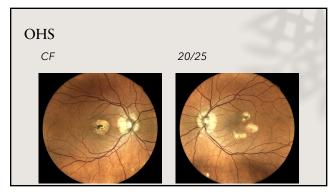
• CNVM OS x 10 years, with 3 injections, VA stable since,

≈20/25

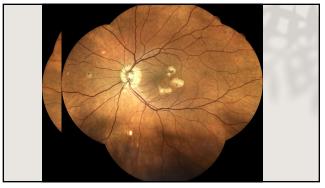
• In for 9 month follow up. Reports stable vision with no active issues

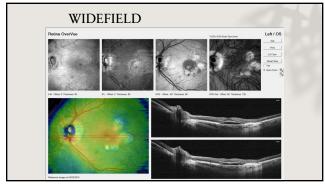
• CF OD

• 20/25 OS

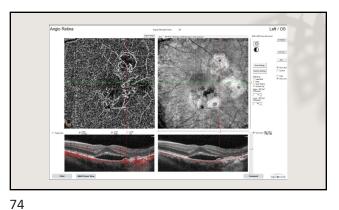


70 71





72 73



65 yo white male

- ASSESSMENT
 - OHS with reactivation CNVM
- PLAN

75

- Avastin x 3
- RTC for repeat OCT, OCTA after 3rd injection
- Pt agrees with plan
- Monoc precautions including Polycarbonate lenses



All you need to know about differentiating ocular histo from toxo

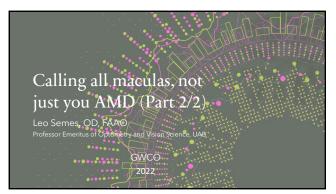
- Histoplasmosis
 - Fungal organism
 - Vector is fowl guano with

 - Affects Lungs OR Eyes
 - Triad of ocular signs • perihpheral "histo spots"
 - parapapillary atrophy
 - macular involvement
 - · Histologically is a primary choroiditis

 - Ocular involvement treat

- Toxoplasmosis
 - Obligate intracellular parasite
- geographic predispositions Vectors are multi (but NOT fowl) with regional predictions
 - Systemic involvement
 - Ocular signs
 - peripheral scarring REACTIVATION
 - · Histologically is a primary

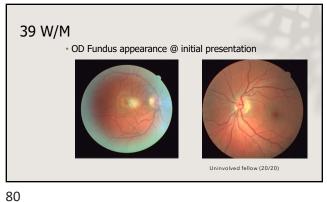
76 77



Case: 39 W/M

- Initial presentation:
 - Desires second opinion on treatment for retinal problem
 - · History: taking clindamycin X 6 weeks PO + steroids PO X 3 weeks (D/C)
- VA (OD) 20/200, mild vitritis, no A/C rxn., all else unremarkable; OS uninvolved
- DDX???

78 79

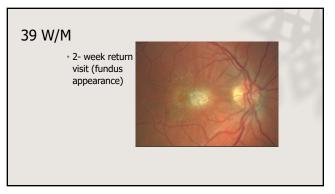


39 W/M

- Initial treatment
 - Bactrim DS (160 mg. Trimethoprim + 800 mg. Sulfmethoxizole)* PO bid X 2 weeks
 - RTC X 2 wks

Current recommended treatment when offered. Lima GSC, Saraiva PGC, Saraiva FP. Current therapy of acquired ocular toxoplasmosis: a review. J O P T. 2015 (Sep): 511-517.

81



39 W/M

- VA unchanged
 - Vitritis slightly diminished
 - Fundus appearance essentially unchanged
 - Options
 - Continue meds???
 - Change meds???Add meds???

· Refer???

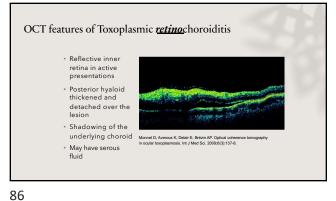
82 83



39 W/M

- •8-week return
 - Patient C/O itch on shoulders and back
 - VA 20/100
 - A/C reaction resolved
 - Fundus remodeling apparent
 - Now what ???

84 85



Management of Ocular Toxoplasmosis

- Clinical Presentation / Diagnosis
 - Observation of a yellowish lesion with overlying inflammatory cells is almost diagnostic
 - · Vitritis/choroiditis may accompany
 - Blood tests are definitive (systemic) but not in ocular
 Sabin-Feldman methylene blue dye test, IgG, IgM, ELISA)
 - Treatment is indicated when the posterior pole is involved

87

Ocular Toxoplasmosis

- 30% 50% of all cases of posterior uveitis
- Clinical presentation (same for cong. and acq.)
 - Focus of necrotizing retinitis
 - Moderate to severe vitritis
 - In immunocompromised patients, there may be multiple foci or extensive necrosis

Ocular Toxoplasmosis

- Clinical epidemiology
 - 1 billion infections worldwide
 - · More prevalent in tropical climates
 - US seropositivity: 3-70% of adults
 - Prevalence 6%
 - · Ratio: acq. 10X more common than cong

Da-la-Torre A, et al. Screening by ophthalmoscopy for *Toxoplasma* retinochoroiditis in *Columbia*. Am J Ophthalmol 2007; 143: 354.

88 89

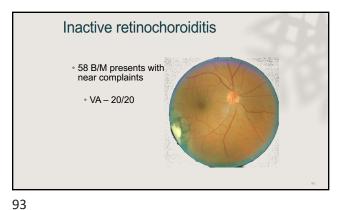
Other Toxoplasmic Retinochoroiditis Risks

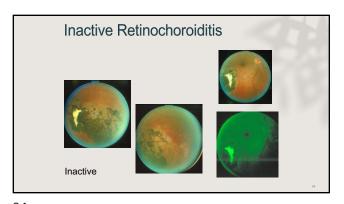
- Eating locally produced cured, dried, or smoked meat
- · Working with meat
- · Drinking unpasteurized goat's milk
- · Having 3 or more kittens
- · Eating raw oysters, clams, or mussels was significant in a separate model among persons asked this question.

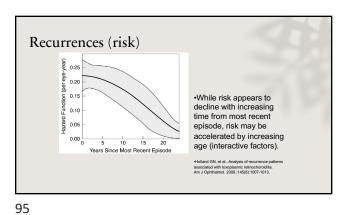
Post-inflammatory lesions

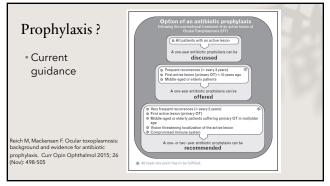
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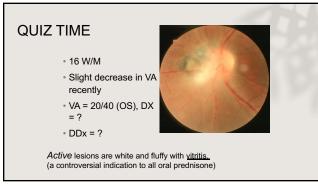


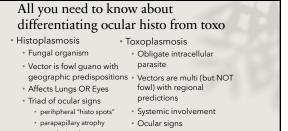












macular involvement

 Histologically is a primary choroiditis

• Ocular involvement - treat

Ocular Toxoplasmosis

• Questions

• Comments

DECAF COFFEE IS

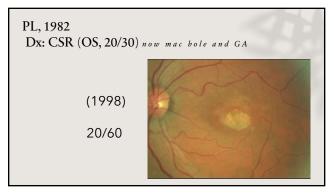
DEPRESSO

98 99

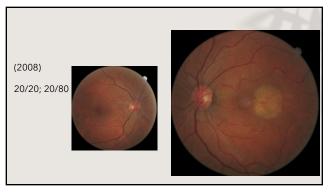
peripheral scarring
 REACTIVATION

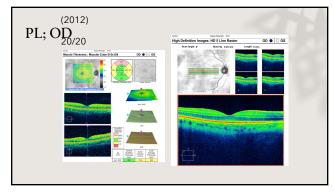
Histologically is a primary

PL, 1982 Dx: CSR (OS, 20/30) now mac hole and GA (1998) 20/60

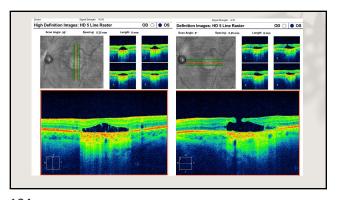


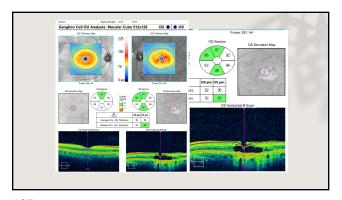
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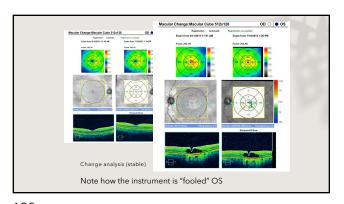




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"...central serous is not an innocuous disease."
R. Morris, MD (c. 1982)
("Retinologist")

106 107

Let's look at an acute case

46 Asian Male

- "blurry vision"
 - X 3 mo OS; began only last night OD
- Began new BP med last week
- Has never had eye exam
- Central blur in OS has improved somewhat
- + floaters X 1 yr
- - flashes, discharge, pain

108 109

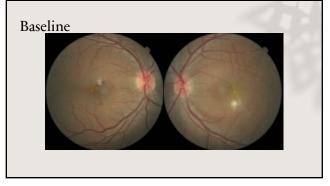
46 Asian Male

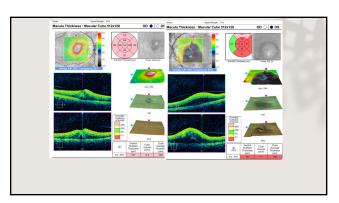
- Previous ocular history is negative for refractive correction, injury, glaucoma, cataract, strabismus, amblyopia, etc.
- Family medical / ocular histories negative
- No known allergies
- Began lisinopril qD X 1 wk. [ACE inhibitor]
- BP 150/100

46 Asian Male

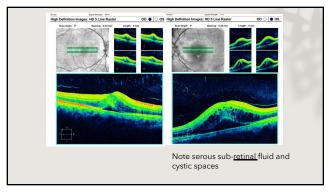
- VA 20/40- 20/400 (PHNI)
- RAPD
- IOP: 14/14
- No EOM restrictions
- Confrontation FTFC OD, OS
- -1.50 / -2.25 -0.50 X 070 VA NI
- Anterior segment unremarkable OD, OS

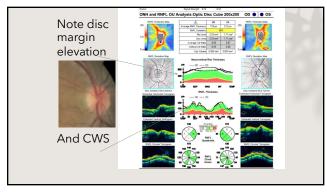
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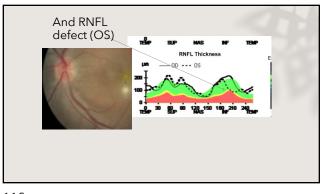


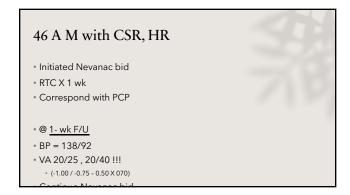
112 113





114 115





46 A M with CSR, HR

Initiated Nevanac bid

© 2- wk F/U

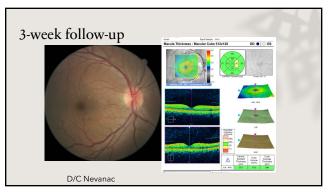
BP = 140/92

VA 20/20-, 20/20-!!!

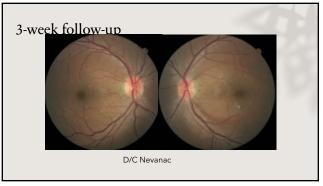
(refraction unchanged)

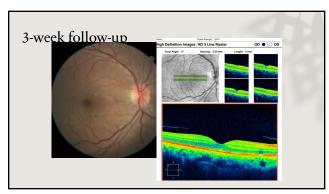
Continue Nevanac bid

RTC X 1 Wk

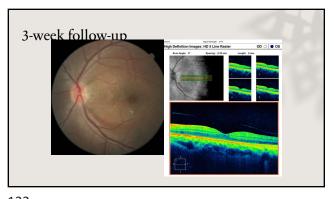


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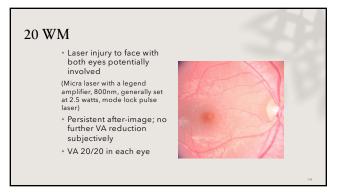


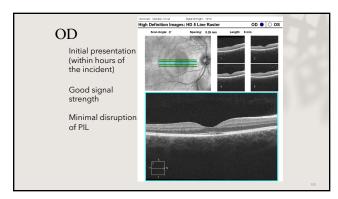


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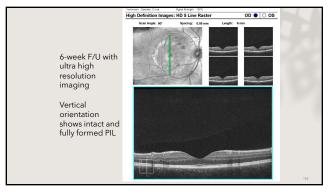


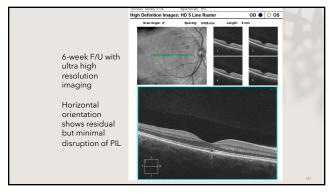






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126 127

Lead of the Committee o

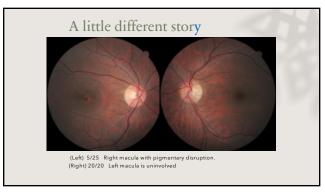
T cases over 2 years; mean age 18.7 yrs (12-26)
Exposure: several seconds, 5mW green laser pointer
Presenting VA range: 20/20 to CF; all reported central/paracentral soctomata.

Distance from source, spot size were not recorded.

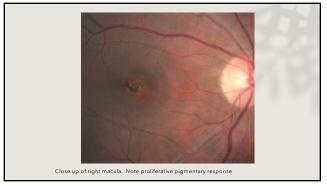
(MPE calculation was, therefore, impossible)

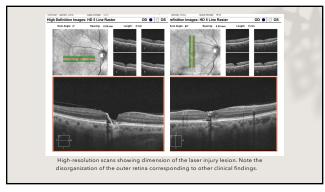
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Summary • 5 eyes showed ophthalmoscopic signs of round retinal discoloration (yellowish/orange)at the macula • 2 eyes showed macular subhyaloid hemorrhage • 1 eye had FTMH with CME • Baseline SD-OCT revealed disruption of the PIL/ellipsoid zone band, and extended toward the inner aspect of the RPE band. • Treatment = oral steroids 0.5 mg/kg/day.(e.g. 40 mg/80Kg) • All but two eyes returned to 20/20 (20/40, CF 2 m.) • Follow-up 2-12 mo.

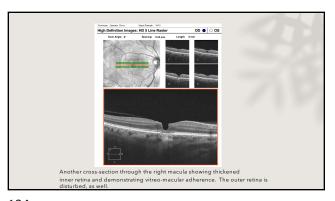


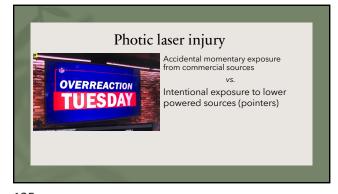
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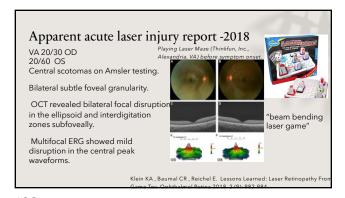


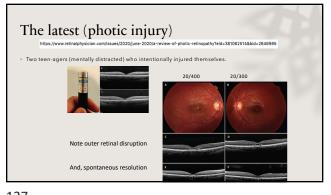


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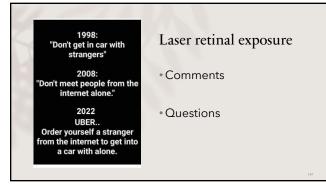






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